

Product Data Sheet

Product Name: Liproxstatin-1

Cat. No.: GC15681

Chemical Properties

Cas. No. 950455-15-9

Chemical Name N-(3-chlorobenzyl)-4'H-spiro[piperidine-4,3'-quinoxalin]-2'-amine

SMILES C1C=CC(CNC(C2(CCNCC2)N3)=NC4=C3C=CC=C4)=CC=C1

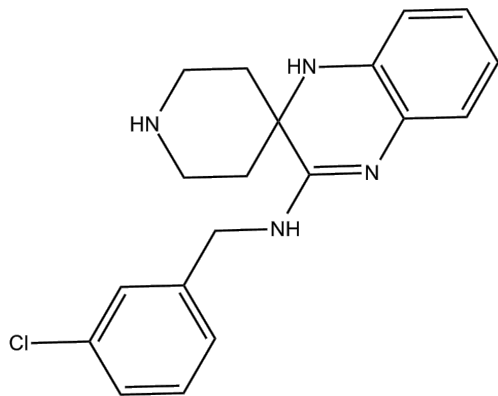
Formula $C_{19}H_{21}ClN_4$ M.Wt 340.85

Solubility $\geq 10.5\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines

K562 cells (human chronic myeloid leukemia cell line)

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Preparation Method	K562 cells were maintained in RPMI-1640 medium supplemented with 10% fetal bovine serum, 100U/ml penicillin and 100µg/ml streptomycin at 37°C, 5% CO ₂ . K562 cells were treated with Liproxstatin-1 at 2-40µM for 24 or 48 hours for viability assay; at 10 or 20µM for 24 hours for cell cycle, Annexin V-FITC/PI staining, TUNEL, immunofluorescence, western blotting, RT-qPCR, TNF-α ELISA and caspase-3/caspase-1 activity assays; at 10 or 20µM for 12 hours for caspase-3/caspase-1 activity assay; at 20µM for 12 hours after 200µM z-DEVD-FMK pretreatment for 3 hours for viability rescue and cleaved N-terminal GSDME detection; and at 10 or 20µM for 24 hours for RNA sequencing.
Reaction Conditions	2-40µM; 12-48h
Applications	Liproxstatin-1 inhibited K562 cell proliferation in a dose- and time-dependent manner. Liproxstatin-1 arrested cell cycle at G1 phase and at G2/M phase under higher concentration. Liproxstatin-1 upregulated p21WAF1/CIP1, BAX, TNF-α, CHOP, PUMA, LC3B and GSDME mRNA levels. Liproxstatin-1 activated caspase-3, cleaved PARP, increased cleaved N-terminal GSDME protein, induced DNA fragmentation, cell swelling, plasma membrane rupture, expanded rough endoplasmic reticulum and increased autolysosomes. Liproxstatin-1 increased caspase-3 activity but not caspase-1 activity. Liproxstatin-1 reduced cell viability partially reversible by z-DEVD-FMK and reduced cleaved N-terminal GSDME upon z-DEVD-FMK cotreatment.
Animal experiment [2]:	
Animal models	8-week-old male C57BL/6 mice

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Preparation Method	Mice were intratracheally injected with bleomycin (3.5mg/kg in 50μL) on day 0. Half an hour before intratracheal injection, mice were intraperitoneally injected with Liproxstatin-1 (0.5μg/μl, 10μg/g) or normal saline, and the intraperitoneal injection of Liproxstatin-1 (10μg/g) was continued once daily from day 0 to day 21. On day 21, mice were sacrificed for lung tissue, serum and bronchoalveolar lavage fluid collection; histopathology (H&E, Masson, Sirius red), immunofluorescence, ELISA, oxidative stress assays (ROS, MDA, GSH, CAT, T-SOD), western blot, and transmission electron microscopy were performed.
Dosage form	10μg/g; i.p.; once daily for 21 days
Applications	Liproxstatin-1 reduced bleomycin-induced elevations of TGF-β1, TNF-α, IL-6 and IL-10 in bronchoalveolar lavage fluid. Liproxstatin-1 reduced lung tissue ROS and MDA levels and increased GSH, CAT and T-SOD activities. Liproxstatin-1 reduced hemorrhagic, vascular congestive, inflammatory infiltrative, epithelial damaging, collagen depositive and alveolar structural chaotic changes in lung tissue. Liproxstatin-1 reduced mitochondrial cristae rupture, swelling and vacuolization in lung tissue under transmission electron microscopy. Liproxstatin-1 downregulated p53 and α-SMA protein expression in lung tissue.
References: [1] Dong H, Liang S, Xu Y, et al. Liproxstatin-1 induces cell cycle arrest, apoptosis, and caspase-3/GSDME-dependent secondary pyroptosis in K562 cells. <i>Int J Oncol.</i> 2022;61(4):119. [2] Tao N, Li K, Liu J, et al. Liproxstatin-1 alleviates bleomycin-induced alveolar epithelial cells injury and mice pulmonary fibrosis via attenuating inflammation, reshaping redox equilibrium, and suppressing ROS/p53/α-SMA pathway. <i>Biochem Biophys Res Commun.</i> 2021 Apr 2;551:133-139.	

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Background

Liproxstatin-1 is a highly efficient and selective ferroptosis inhibitor with an IC₅₀ of 22nM.

Liproxstatin-1 inhibits lipid autoxidation by capturing peroxy radicals, blocks iron-dependent programmed cell death, and restores the expression of glutathione peroxidase 4 and ferroptosis suppressor protein 1. Liproxstatin-1 can be used for research related to ferroptosis mechanisms, ischemia-reperfusion injury, neurodegenerative diseases, and acute kidney injury^[1-4].

In vitro, treatment of K562 cells with 2-40μM Liproxstatin-1 for 24-48 hours dose- and time-dependently inhibited cell proliferation, arrested the cell cycle at G1 phase, and induced DNA fragmentation^[5]. Co-treatment of human HK2 cells with 0.5μM Liproxstatin-1 and 1.0μM RSL3 for 24 hours protected HK2 cells from RSL3-induced injury, reduced intracellular iron concentration and MDA levels, and decreased secretion of TGF-β, CTGF and PDGF in culture supernatant^[6]. Co-treatment of BEAS-2B cells with 5μM Liproxstatin-1 and 10μg/mL bleomycin for 24-84 hours prevented bleomycin-triggered cell death and reduced intracellular reactive oxygen species levels^[7].

In vivo, intraperitoneal injection of 10μg/g Liproxstatin-1 every two days (4 total injections) in a neutrophilic asthma C57BL/6J mouse model reduced peribronchial and perivascular inflammatory cell infiltration, inhibited airway mucus secretion, and decreased neutrophils, eosinophils, lymphocytes, macrophages and total cell counts in bronchoalveolar lavage fluid^[8]. Intraperitoneal injection of 10mg/kg Liproxstatin-1 for 2 consecutive weeks in a metabolic-associated fatty liver disease C57BL/6J mouse model reduced hepatic triglyceride and cholesterol levels, decreased liver lipid peroxidation markers 4-HNE and MDA, and alleviated lipid droplet deposition^[9]. Daily intraperitoneal injection of 10μg/g Liproxstatin-1 starting 0.5 hours before intratracheal instillation of bleomycin (3.5mg/kg) for 21 consecutive days in C57BL/6 mice reduced pulmonary hemorrhage, vascular congestion, inflammatory cell infiltration, epithelial injury and collagen deposition, and improved mitochondrial ultrastructural abnormalities^[10].

References:

[1] Zilka O, Shah R, Li B, et al. On the Mechanism of Cytoprotection by Ferrostatin-1 and Liproxstatin-1 and the Role of Lipid Peroxidation in Ferroptotic Cell Death. ACS Cent Sci. 2017 Mar 22;3(3):232-243.

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- [2] Cao JY, Dixon SJ. Mechanisms of ferroptosis. *Cell Mol Life Sci.* 2016 Jun;73(11-12):2195-209.
- [3] Shi Z, Du Y, Zheng J, et al. Liproxstatin-1 Alleviated Ischemia/Reperfusion-Induced Acute Kidney Injury via Inhibiting Ferroptosis. *Antioxidants (Basel).* 2024 Jan 31;13(2):182.
- [4] Zhao J, Li J, Wei D, et al. Liproxstatin-1 Alleviates Lung Transplantation-induced Cold Ischemia-Reperfusion Injury by Inhibiting Ferroptosis. *Transplantation.* 2023 Oct 1;107(10):2190-2202.
- [5] Dong H, Liang S, Xu Y, et al. Liproxstatin-1 induces cell cycle arrest, apoptosis, and caspase-3/GSDME-dependent secondary pyroptosis in K562 cells. *Int J Oncol.* 2022;61(4):119.
- [6] Zhang B, Chen X, Ru F, et al. Liproxstatin-1 attenuates unilateral ureteral obstruction-induced renal fibrosis by inhibiting renal tubular epithelial cells ferroptosis. *Cell Death Dis.* 2021 Sep 11;12(9):843.
- [7] Pei Z, Qin Y, Fu X, et al. Inhibition of ferroptosis and iron accumulation alleviates pulmonary fibrosis in a bleomycin model. *Redox Biol.* 2022;57:102509.
- [8] Bao C, Liu C, Liu Q, et al. Liproxstatin-1 alleviates LPS/IL-13-induced bronchial epithelial cell injury and neutrophilic asthma in mice by inhibiting ferroptosis. *Int Immunopharmacol.* 2022 Aug;109:108770.
- [9] Tong J, Lan X, Zhang Z, et al. Ferroptosis inhibitor liproxstatin-1 alleviates metabolic dysfunction-associated fatty liver disease in mice: potential involvement of PANoptosis. *Acta Pharmacol Sin.* 2023;44(5):1014-28.
- [10] Tao N, Li K, Liu J, et al. Liproxstatin-1 alleviates bleomycin-induced alveolar epithelial cells injury and mice pulmonary fibrosis via attenuating inflammation, reshaping redox equilibrium, and suppressing ROS/p53/ α -SMA pathway. *Biochem Biophys Res Commun.* 2021 Apr 2;551:133-139.

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